Remarks

Claims 1-52 are pending. Claim 1 has been amended. Claims 6-52 have been withdrawn from consideration as being drawn to a non-elected invention. Claim 53 is newly added. New claim 53 finds support in the specification on page 23, paragraph 92, lines 23-27.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-5 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Office Action states that no support for step c) of claim 1 was provided by the applicant in the previous response. Applicants note that paragraph 45 (page 14, lines 8-9) of the current specification provides support. The specification states that "screening means identifying the presence of a property." Therefore, since the mere meaning of screening is identifying then this definition provides support for the step of identifying in c).

Applicants respectfully request withdrawal of the 35 U.S.C. § 112 rejection.

Rejection Under 35 U.S.C. § 102

Claims 1-5 were rejected under 35 U.S.C. § 102(e) as being anticipated by Thompson (U.S. Patent 7,029,859). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Thompson treaches methods for detecting, diagnosing and treating metastatic disorders and how caveolin expression correlates with metastasis. Thompson does not teach about breast cancer and how androgen receptor correlates with breast cancer. The only place where Thompson mentions "androgen receptor" is in Example 2, and Thompson provides a correlation between caveolin and androgen/androgen receptor in castration-induced regression of mouse prostate cancer (Col 23, lines 4-17). This is done in a castration mouse model, having nothing to do with breast cancer or breast tissue. Therefore, the implication that Thompson could possibly anticipate the current claims focused on androgen receptor and breast cancer is illogical.

As stated in 35 U.S.C. 102(e):

> A person shall be entitled to a patent unless-
>
> > The invention was described in -- ....a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent....

And as stated in the MPEP §2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art."

The Office Action alleges that there are only two active steps in the claim and thus does not give patentable weight to the last limitation in step c. The two steps given patentable weight are a) obtaining a tissue sample and b) assaying for the presence of the androgen receptor. Applicants note however that the other limitation found in step b) "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer" was not acknowledged by the Examiner. This limitation is a clear difference between the claimed invention and Thompson. Applicant is not sure why this limitation was overlooked by the Examiner but in the case that the Examiner did not consider this limitation due to an alleged lack of patentable weight, arguments are provided below.

First, it is clear that "wherein" and "whereby" clauses are not automatically (or even often) excluded as true limitations. For example, when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention" (*Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 74 USPQ2d 1481 (Fed. Cir. 2005)). In *Hoffer v. Microsoft*, the court stated that if the clause is more than an intended result of a process, for example, it is a part of the process itself, then it should be considered as a limitation to the claim. Applicants assert that the limitation, "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer," is not merely an intended use but is part of the claimed process. By this, Applicants mean that the presence of androgen receptor indicating the presence or risk of breast cancer is part of the method of screening a subject for breast cancer and is not merely a result of the screen. Thus, this limitation is a part of the claimed process. The fact that the limitation requires that the presence of androgen receptor indicates the presence or

risk of breast cancer makes it clear that this limitation is a part of the process itself because in order to screen subjects for breast cancer, one must know that the presence of androgen receptor indicates the presence or risk of breast cancer. Without this limitation, the presence (or absence) of androgen receptor in the screen would seem irrelevant – one must know that the presence of androgen receptor indicates risk or presence of breast cancer.

The claimed method of screening a subject for breast cancer requires that the presence of androgen receptor indicates the presence or risk of breast cancer. In other words, the method requires determining that breast cancer or the risk thereof is present. The method of screening does not *result* in the presence of androgen receptor indicating the risk or presence of breast cancer. Instead, the method of screening includes the determination of the presence or risk of breast cancer based on the presence of androgen receptor. Thus, the 'whereby' clause is a part of the method and not a result of the method and thus must be considered when determining patentability. Thompson in no way teaches that the presence of androgen receptor indicates the presence or risk of breast cancer. Since Thompson does not teach the presence of androgen receptor in breast cancer, he can not possibly teach that androgen receptor could be used as an indicator of breast cancer. Thus, upon consideration of the limitation in step b) stating "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer," Applicants request that the Examiner withdraw the anticipation rejection as every element of the currenct claims are not taught by Thompson.

If the examiner does not give patentable weight to the 'wherein' clause from step b), then there is no question that step c) adds substance to the claim and is not simply a result of the other two steps. The limitation of step c) in claim 1 recites " identifying the subject as having a increased risk of breast cancer when the presence of androgen receptor is identifed" and this limitation is being focused on by the Examiner. The Office Action states that claim 1, step c) "merely states the results of the two limitations or steps in the claim and adds nothing to the patentability or substance of the claim." If the first two steps were simply obtaining a tissue sample and assaying for the presence of androgen receptor, then the result of these steps would be either finding or not finding androgen receptor in the sample. Correlating the presence of androgen receptor to an increased risk of or presence of breast cancer, as done in step c), would

not be a simple result of those steps. Determining the presence of androgen receptor in a sample does not result in the identification of a subject with breast cancer or the risk thereof. One must make a specific effort to do the step of identifying and thus it is part of the process (method) and not a result of the process. For example, if the steps were a) obtain a sample, b) assay for androgen receptor and c) determine/identify the presence of androgen receptor, then one might allege that step c) is simply a result of the other two steps and not a part of the process. Determining the presence of androgen receptor could be a result of obtaining a sample and assaying for the androgen receptor. However, the step of identifying a subject as having breast cancer or a risk of breast cancer based on the presence of androgen receptor is not a result but an actual step.

Lastly, there can be no doubt that steps b) and c) are material to patentability, as there is no doubt that the set of actors of the method of claim 1 is a different set if only steps a) and b) are completed than the set of actors if steps a), b), and c) are completed. One can perform steps a) and b), and not identify the a subject as in step c). If a claim requires one to identify a subject, clearly the set of actors of the claim is different than if the claim only required steps a) and b). There can be no higher indication of materiality. Clearly if step c) changes the scope of the claim from what it would be without step c), step c) must be considered a meaningful limitation.

Applicants conclude that both step c) and the wherein clause of step b) are limitations that provide a clear difference between the claimed invention and Thompson. Therefore, Applicants request withdrawal of the 35 U.S.C. § 102(e) rejection.

Claims 1-5 were rejected under 35 U.S.C. § 102(b) as being anticipated by Fujimoto et al. (Laboratory Investigation 80:1465-1471, 2000). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Fujimoto et al. describe the expression of androgen receptor in advanced Extramammary Paget's Disease (EMPD). Fujimoto et al. do not teach the presence of androgen receptor being indicative of an increased risk or presence of breast cancer, as their disclosure is on EMPD not breast cancer. EMPD is not breast cancer and does not teach or suggest breast cancer. Therefore, every element of the current claims are not found in the alleged prior art.

As stated in 35 U.S.C. 102(b):

> A person shall be entitled to a patent unless-
>
> > The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

And as stated in the MPEP §2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art."

Fujimoto et al. assay tissue samples for androgen receptor and indicate that androgen receptor is one of the hormone receptors responsible for the development and growth of EMPD. A tissue sample is obtained and androgen receptor is assayed for but Fujimoto et al. clearly describes this with regards to EMPD, not breast cancer.

The current claims specifically state the limitation of "...wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer." The rejection infers that this "wherein" clause is not part of the active step stated in the claims and that step c) reciting "identifying the subject as having a increased risk of breast cancer when the presence of androgen receptor is identifed" is not given patentable weight and therefore does not have to be met by the cited art.

Applicants refer to their arguments above related to the Thompon rejection in which they state that the presence of androgen receptor indicating the presence or increased risk of breast cancer is not a result of the method but in fact, is a part of the method and therefore should be given patentable weight. Not only is this "wherein" clause a required limitation, but step c) in claim 1 requires the correlation between androgen receptor and presence or risk of breast cancer. Since Fujimoto does not teach a correlation between androgen receptor and breast cancer, it fails to satisfy 35 U.S.C. § 102(b) and therefore these claims are not anticipated. Applicants request that the examiner should give patentable weight to all of these limitations and thus withdraw the current rejection.

Claims 1-5 were rejected under 35 U.S.C. § 102(a) as being anticipated by Moinfar et al. (Cancer 98:703-711, 2003). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Moinfar et al. investigated the expression of androgen receptor in breast carcinomas and described the correlations with other hormone receptors and Her-2 expression. Moinfar et al. do *not* describe a correlation between androgen receptor and the increased risk or presence of breast cancer. Therefore, every element of the current claims are not found in the alleged prior art.

As stated in 35 U.S.C. 102(a):

> A person shall be entitled to a patent unless-
>
> > The invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.

And as stated in the MPEP §2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art."

Applicants assert that Moinfar et al. do not teach that the presence of androgen receptor indicates the presence or increased risk of breast cancer. In fact, they appear to teach the opposite of this by showing that androgen receptor is not a good marker for tumor progression.

Moinfar states,

> The aim of the current study was to investigate the expression of AR in a large series of breast carcinomas using immunohistochemical techniques. The results were analyzed for correlations with ER, PR, and HER-2/neu expression, as determined immunohistochemically in tissue sections from paraffin-embedded archival material. Page 704, 1st column

Note that the "aim" was not to identify AR as a prognosticator, but to "analyze correlations with ER, PR, and Her2/neu."

Again, the Office Action alleges that the limitation of the presence of androgen receptor indicating the presence or increased risk of breast cancer is not an active step and thus not given patentable weight. Applicants past arguments for the difference between the cited art and the claimed invention have focused on this claim limitation because Moinfar et al. clearly do not

correlate androgen receptor to the presence or risk of breast cancer but rather correlate androgen receptor to other proteins. Thus Applicants herein provide support for the patentable weight of this limitation.

Applicants direct the examiner to their arguments provided above under the Thompson rejection as to why the limitation of the presence of androgen receptor indicating the presence or risk of breast cancer should be given patentable weight. Briefly, in claim 1, step b), the limitation "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer" is part of the method of screening and not a result of the screen and therefore should be given patentable weight. Furthermore, if that limitation is not considered part of the active steps, then there is no question that step c) should be considered and would not simply be a result of step a and step b.

Upon consideration of the limitation of the presence of androgen receptor indicating the presence or risk of breast cancer, it is clear that Moinfar et al. do not teach this element of the current claims and therefore can not anticipate the claimed invention. As stated previously, Moifar et al. teach a correlation between androgen receptor and ER, PR and HER-2 expression. There is no teaching that the presence of androgen receptor indicates the presence or risk of breast cancer. In fact, Moinfar et al. only look at androgen receptor in cancer cells/tissue. They do not teach the presence or absence of androgen receptor in normal or healthy tissue. Without comparing the presence of androgen receptor in cancerous tissue to a healthy tissue, one of skill in the art could not determine if androgen receptor indicates the presence or risk of breast cancer.

Rejection Under 35 U.S.C. § 103

Claims 1-5 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Fujimoto et al., in view of Thompson. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The rejection relies on Fujimoto et al. for teaching the expression of androgen receptor. The rejection alleges the only deficiency of Fujimoto et al. is the lack of teaching of the subject being a mouse. Thus, the Examiner relies on Thompson et al. to teach assaying androgen receptor in a rodent. However, Fujimoto et al. teach androgen receptor in EMPD, not breast cancer and Thompson teaches androgen receptor in a prostate cancer model, not breast cancer.

Therefore, there is no correlation between androgen receptor and breast cancer being taught in either of these references alone, much less a combination of the two of them.

Claims 1-5 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Moinfar et al., in view of Thompson. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The rejection relies on Moinfar et al. for teaching the expression of androgen receptor. The rejection alleges the only deficiency of Moinfar et al. is the lack of teaching of the subject being a mouse and a male. Thus, the Examiner relies on Thompson et al. to teach assaying androgen receptor in a rodent and in males. However, Moinfar et al. teach expression of androgen receptor in breast carcinomas and describe the correlations with other hormone receptors and Her-2 expression, not a correlation with the presence or risk of breast cancer. Thompson teaches androgen receptor in a prostate cancer model, not breast cancer. Therefore, there is no correlation between androgen receptor and breast cancer being taught in either of these references alone, much less a combination of the two of them.

In order to establish a *prima facie* case of obviousness, the burden is on the examiner to show that the prior art provides a suggestion or motivation to modify or combine the cited references and there must be a reasonable expectation of success. Showing a motivation to combine these references is important to prevent the combination of references which would not otherwise be combined, but for hindsight. It is also important to show that the combination of references would have led to reasonable expectation of success. The Office has not done this here. The examiner has failed to provide the appropriate motivation linked to the reasonable expectation of success required by the chemical case law post *KSR*.

A. The Law

No where is there a suggestion or motivation to combine Fujimoto et al. and Thompson or Moinfar et al. an dThompson. The Supreme Court in *KSR v Teleflex*, indicated that a teaching, suggestion, or motivation while not absolutely required could be useful in certain types of technologies as well as a reasonable expectation of success *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 396, 127 S. Ct. 1727 (2007). The Federal Circuit has expanded from this, particularly in the area of chemical and biotechnology inventions.

The Federal Circuit has held that a reasonable expectation of success should be present for a "composition" to be obvious under *KSR* and that the unpredictability of pharmaceutical compositions makes this a difficult hurdle to clear.

The Federal Circuit has found

> [To find a composition obvious a court must find that] . . .a person having ordinary skill in the art would have had "reason to attempt to make the composition" known as risedronate and "a reasonable expectation of success in doing so.

PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360 (Fed. Cir. 2007)." Furthermore, the Federal Circuit has indicated that to determine whether a composition which was a derivative was obvious, a showing that the specific modifications would have been suggested is needed. (See *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008), *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007), and *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985)).

The Federal Circuit has also focused on unpredictability as an indicator of a lack of expectation of success. (See *Proctor & Gamble Comp. v. Teva Pharmaceuticals USA Inc.*, Slip opinion 2008-1404, 1406, and 1408 (Fed. Cir. 2009).

The Federal Circuit stated in *Eisai*,

> "The Supreme Court's analysis in KSR thus relies on several assumptions about the prior art landscape. First, KSR assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions." In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008), this court further explained that this "easily traversed, small and finite number of

> alternatives . . . might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable."

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Thus, the current chemical case law clearly indicates that there should be a teaching, suggestion or motivation as well as a reasonable expectation of success for a chemical composition to be obvious.

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 127 S.Ct. 1727, 1741 (2007). Applicant emphasizes that there must be a suggestion or motivation to combine the cited art. In support of the fact that there was no motivation to combine the cited art, the examiner is directed to *Takeda Chem. Indus., Ltd v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1357* (Fed. Cir. 2007). Takeda started with a known compound and substituted a methyl group for an ethyl group at one position. The Federal Circuit affirmed the District Court's decision that Takeda's compound was not obvious. The court relied on an expert's admission that the skilled artisan would "look at a host of substituents, such as chlorides, halides and others, not just methyls" when making their modifications. Thus, under KSR Int'l Co. v. Teleflex Inc., "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda, Id.*

B. No *prima facie* case

1. Fujimoto et al. and Thompson

The present method of screening claims comprise three elements 1) obtaining a tissue sample, 2) assaying for the presence of androgen receptor, wherein the presence of androgen recpetor indicates an increased risk of or presence of breast cancer, and 3) identifying the subject as having an increased risk of breast cancer when the presence of androgen receptor is identified. There has been no showing by the Examiner that there would have been a motivation to combine the art to provide these elements. Additionally, the Examiner has not provided

evidence that there would have been a reasonable expectation of success in combining all of the elements referenced in the prior art in order to result in the claimed composition, and thus the Examiner has failed to make a *prima facie* case of obviousness as required.

The current claimed invention is a method of screening comprising "a) obtaining a tissue sample, b) assaying for the presence of androgen receptor, wherein the presence of androgen recpetor indicates an increased risk of or presence of breast cancer, and c) identifying the subject as having an increased risk of breast cancer when the presence of androgen receptor is identified." This combination of elements is not found in the art nor is there any motivation to combine the art to accomplish these limitations. Just like in *Takeda*, where there was no motivation to modify their compound with that particular substituent, Applicants had no motivation to "modify" their androgen receptor screening assay to correlate to breast cancer. None of the cited art suggested or motivated Applicants to start with Fujimoto et al.'s assaying of androgen receptor which was performed from tissue of EMPD and end up with the currently claimed screening method which correlates androgen receptor to breast cancer. Thompson does not teach a correlation between androgen receptor and breast cancer and thus does not make up for the deficiency of Fujimoto et al. No where is there an indication to go and find the missing elements, or even a reason to do so. One of skill in the art would not think it was obvious to combine Fujimoto et al. with Thompson because there is no suggestion that there would be a reasonable expectation of success due to Fujimoto et al. teaching about EMPD and Thompson teaching about prostate cancer. The skilled artisan would not have been led to determine a correlation between androgen receptor and breast cancer from these disclosures. The mere identification of androgen receptor in tumors related to a disease other than breast cancer does not make it obvious to assay for the presence of androgen receptor and correlate it with an increased risk of or presence of breast cancer due to the vast differences among different diseases and more importantly among different types of cancer. Of all the diseases that could be investigated and combined with an androgen receptor assay, one of skill in the art would not have thought it was obvious to pick the exact combination as done in the current claims.

The rejection alleges that both Fujimoto et al. and Thompson provide all of the elements of claim 1, 2, 4, 5 and that Thompson allegedly provides the extra limitation of the subject being

a mouse in claim 3. As argued in the 35 U.S.C. § 102 rejections, the limitation providing the correlation between androgen receptor and breast cancer was clearly not given patentable weight but should have been. Upon consideration of the limitation "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer," there is no suggestion or motivation to combine Fujimoto et al. and Thompson – particularly because neither of them teach an increased risk of or presence of breast cancer.

Thus, the Examiner has failed to arrive at a prima facie case of obviousness, and removal of the rejection is earnestly requested.

2. Moinfar et al. and Thompson

The present method of screening claims comprise three elements 1) obtaining a tissue sample, 2) assaying for the presence of androgen receptor, wherein the presence of androgen recpetor indicates an increased risk of or presence of breast cancer, and 3) identifying the subject as having an increased risk of breast cancer when the presence of androgen receptor is identified. There has been no showing by the Examiner that there would have been a motivation to combine the cited art to provide these elements. Additionally, the Examiner has not provided evidence that there would have been a reasonable expectation of success in combining all of the elements referenced in the prior art in order to result in the claimed composition, and thus the Examiner has failed to make a *prima facie* case of obviousness as required.

The current claimed invention is a method of screening comprising "a) obtaining a tissue sample, b) assaying for the presence of androgen receptor, wherein the presence of androgen recpetor indicates an increased risk of or presence of breast cancer, and c) identifying the subject as having an increased risk of breast cancer when the presence of androgen receptor is identified." This combination of elements is not found in the art nor is there any motivation to combine the art to accomplish these limitations. Just like in *Takeda*, where there was no motivation to modify their compound with that particular substituent, Applicants had no motivation to "modify" their androgen receptor screening assay to correlate to breast cancer. None of the cited art suggested or motivated Applicants to start with Moinfar et al.'s correlation of androgen receptor to other hormone receptors and Her-2 and end up with the currently claimed screening method which correlates androgen receptor to the presence or risk of breast

cancer. Thompson does not teach a correlation between androgen receptor and breast cancer and thus does not make up for the deficiency of Moinfar et al. No where is there an indication to go and find the missing elements, or even a reason to do so. One of skill in the art would not think it was obvious to combine Moinfar et al. with Thompson because there is no suggestion that there would be a reasonable expectation of success due to Moinfar et al. teaching a correlation between androgen receptor and hormone receptors and Her-2 and Thompson teaching about prostate cancer. The skilled artisan would not have been led to determine a correlation between androgen receptor and the presence or risk of breast cancer from these disclosures. Of all the things androgeen receptor could be correlated to (or tested for a correlation), one of skill in the art would not have thought it was obvious to pick the exact combination as done in the current claims.

The rejection alleges that both Moinfar et al. and Thompson provide all of the elements of claims 1-5. As argued in the 35 U.S.C. § 102 rejections, the limitation providing the correlation between androgen receptor and breast cancer was clearly not given patentable weight but should have been. Upon consideration of the limitation "wherein the presence of androgen receptor indicates an increased risk of or presence of breast cancer," there is no suggestion or motivation to combine Moinfar et al. and Thompson – particularly because neither of them teach an increased risk of or presence of breast cancer in correlation with androgen receptor.

Thus, the Examiner has failed to arrive at a prima facie case of obviousness, and removal of the rejection is earnestly requested. Notwithstanding this failure, however, Applicants provide below evidence of secondary considerations of non-obviousness demonstrating the clear patentability of the present claims.

i. Teaching away

Not only has a prima facie case of obviousness not been made, other considerations of non-obviousness exist. There is a teaching away from the claimed technology. As stated in the MPEP § 2141.02, "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)."

Furthermore, "[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by applicant" (*United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966)). Thus, as discussed below, comparing androgen receptor to a known breast cancer biomarker and getting an inverse relationship would lead the skilled artisan to believe that the presence of androgen receptor does not correlate with breast cancer.

Applicants assert that Moinfar et al. do not teach that the presence of androgen receptor indicates the presence or increased risk of breast cancer. In fact, they appear to teach the opposite of this by showing that androgen receptor is not a good marker for tumor progression. The first column on page 706 of Moinfar supports this stating,

> Her-2/neu showed an increase in overexpression frequency with increasing tumor grade, from 0% in G1 ICAs, to 26% in G2 ICAs and 42% in G3 ICAs. Page 706, 1st col.

Today, Her-2/neu is one of the most predictive indicators of breast cancer carcinomas, and as proclaimed in Moinfar, AR in breast carcinomas is *decreasing* as the tumor progresses and gets worse. Based on this, the skilled artisan would not think it was obvious to correlate androgen receptor to breast cancer. Since one of the most predictive indicators of breast cancer (Her-2) is expressed more in invasive cancers, one would not think to correlate androgen receptor (shown in Moinfar to be present more in noninvasive cancers) to the presence or risk of breast cancer. Thus, Moinfar teaches away from correlating androgen receptor to the presence of or risk of breast cancer by instead teaching an inverse correlation between a common breast cancer marker (Her-2) and androgen receptor.

Thus, Applicant respectfully traverses this obviousness rejection and requests withdrawal of this rejection.

Claim Objections

Claim 1 was objected to for a grammar informality. Applicants have amended the claim per the examiner's recommendation and thus should overcome the rejection.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A deposit order account charge made electronically in the amount of $470.00, $65.00 representing the fee for a small entity under 37 C.F.R. § 1.17(a)(1), $405.00, representing the fee for a small entity under 37 C.F.R. § 1.17(e), and a Request for Extension of Time and a Request for Continued Examination are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-4667.

Respectfully submitted,

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/David E. Huizenga/

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